REMARKS

The Office Action dated January 13, 2003 presents the examination of claims 1-4 and 13-17. Claims 5-12 are withdrawn from consideration. Claim 16 is canceled. Claims 1, 13, 14, 15, and 17 are amended. Support for the amendment to claim 1 is found on page 15, lines 1-12. No new matter is inserted into the application.

Information Disclosure Statement

Applicants filed an Information Disclosure Statement (IDS) on October 4, 2001. The Examiner is respectfully requested to make the references disclosed therein of record in the present application, by initialing and returning the Form PTO-1449. Another copy of the Form PTO-1449 is attached hereto for the Examiner's convenience.

Election of Species

The Examiner requires Applicants to elect a single species of cyclic GMP phosphodiesterase inhibitors as set forth in claims 13-15. Applicants elect sildenafil with traverse.

First of all, the Examiner is reminded that the present application is the National Stage filing of an international PCT application under 35 U.S.C. § 371. Therefore, restriction practice is governed by 37 C.F.R. § 1.475, Unity of Invention. "Examiners are reminded that unity of invention (not restriction)

practice is applicable in international applications (both Chapter I and II) and in national stage applications submitted under 35 U.S.C. § 371." U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. § 1893.03(d) (8th ed. rev. 1, Feb. 2003).

Under the concept of unity of invention, a single application should relate to a single invention. However, a single application may include more than one invention if the inventions are linked so as to form a single general inventive concept. See, PCT Rule 13.1. A group of inventions is considered lined so as to form a single general invention concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. See, PCT Rule 13.2.

The Examiner's attention is drawn in particular to Annex B of the MPEP, which provides instructions concerning unity of invention. Claims 13, 14, and 15 are directed to Markush groups. On page AI-64, it is noted that "Markush practice," wherein a single claim defines alternatives (chemical or non-chemical), is governed by Rule 13.2.

> When a Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:
>
> (A) all alternatives have a common property or activity, and
>
> (B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives, or
>
> (B)(2) in cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

U.S. Pat. & Trademark Off., Manual Pat. Examining Proc. Annex B, Unity of Invention, Part 1 (8th ed. rev. 1, Feb. 2003).

In the present case, all elements for unity of invention of a Markush group are met. First, all members of the chemical group have the same activity, i.e., they are all cyclic GMP phosphodiesterase inhibitors. Second, all members of the chemical group share a common structure, i.e., a pyridazine group. Third or alternatively, all members belong to a recognized class of chemical compounds in the art to which the invention pertains, i.e., they are all cyclic GMP phosphodiesterase inhibitors. For these reasons, it is clear that the compounds of claims 13, 14, and 15 have unity of invention under PCT Rules 13.1 and 13.2. The Examiner is reminded that even if alternatives of a Markush grouping can be differently classified, this fact, taken alone, is not considered to be justification for a finding of lack of unity of invention. For these reasons, the election of species requirement is clearly improper and should be withdrawn. Reconsideration of the claims and withdrawal of the instant election of species requirement are respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejects claims 13-15 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter not

described in the specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Claim 13

The Examiner states that the structural formulas set forth in claims 13-15 are not disclosed in the specification, but since they are a part of the original disclosure, may be inserted into the specification. In response to the Examiner's remarks, Applicants amend the specification accordingly. Thus, the instant rejection is overcome.

Claim 14

The Examiner asserts that claim 14 is not commensurate in scope with the disclosure because it recites a substitution without describing the particular effective substituent. Applicants amend claim 14 to clarify that substituents.

Applicants respectfully submit that the instant claims fully comply with 35 U.S.C. § 112, first paragraph. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claim 14 under 35 U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants respectfully

traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner states that the phrases "for example" and "i.e." render claim 14 indefinite. Claim 14 is amended to remove these phrases. Thus, the instant rejection is overcome.

Claim Objections

The Examiner objects to claims 16 and 17 under 37 C.F.R. § 1.75(c) for being improper multiple dependent claims. Claim 16 is canceled, thus rendering rejection thereof moot. Applicants respectfully traverse the rejection applied to claim 17. Reconsideration of the claim and withdrawal of the instant rejection are respectfully requested.

Claims 17 is amended into proper multiple dependent form. Thus, the instant objection is overcome.

Rejection under 35 U.S.C. § 102(b)

WO '675

The Examiner rejects claims 1-4 and 13 under 35 U.S.C. § 102(b) for allegedly being anticipated by WO '675 (WO 97/03675). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

WO '675 discloses the use of cGMP-phosphodiesterase inhibitors to treat impotence. WO '675 discloses that the compounds may be administered in the form of a tablet containing

excipients such as starch or lactose. However, WO '675 fails to disclose an intraoral quickly disintegrating tablet comprising a cyclic GMP phosphodiesterase inhibitor and a saccharide selected from the group consisting of mannitol, xylitol, and erythritol, wherein the saccharide is present in a ratio of 4 to 30 parts by weight to 1 part by weight of the cyclic GMP phosphodiesterase inhibitor, as recited in the amended claim 1.

The larger amount of sugar alcohol as claimed in the present invention provides unexpected superior results. Specifically, the tablet of the present invention rapidly disintegrates in the mouth compared to tablets of the prior art, which do not contain such a high amount of sugar alcohol. As shown in Figure 4 of the specification, the tablet of the present invention disintegrates much more quickly and the medicine is eluted at a higher percentage at any pH value, when compared to a tablet prepared by the conventional method.

For these reasons, WO '675 fails to anticipate the present invention. Withdrawal of the instant rejection is therefore respectfully requested.

EP '626

The Examiner rejects claims 1-4 and 13 under 35 U.S.C. § 102(b) for allegedly being anticipated by EP '626 (EP 0 636 626 A1[1]). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully

[1] The Examiner refers to the prior art as EP 0 636 628 A1. Applicants assume

requested.

EP '626 discloses pyrazolopyrimidine derivatives. EP '626 discloses that the compound may be administered in the form of tablets containing excipients such as starch or lactose. However, EP '626 fails to disclose an intraoral quickly disintegrating tablet comprising a cyclic GMP phosphodiesterase inhibitor and a saccharide selected from the group consisting of mannitol, xylitol, and erythritol, wherein the saccharide is present in a ratio of 4 to 30 parts by weight to 1 part by weight of the cyclic GMP phosphodiesterase inhibitor, as recited in the amended claim 1.

Thus, EP '626 fails to anticipate the present invention. Withdrawal of the rejection is therefore respectfully requested.

Bell-Huff '172

The Examiner rejects claims 1-4 and 13 under 35 U.S.C. § 102(e) for allegedly being anticipated by Bell-Huff '172 (US 2002/0002172 A1). Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Bell-Huff '172 discloses rapidly disintegrating pharmaceutical preparations of sildenafil. However, Bell-Huff '172 fails to disclose an intraoral quickly disintegrating tablet comprising a cyclic GMP phosphodiesterase inhibitor and a saccharide selected from the group consisting of mannitol,

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that this is a typographical error.

xylitol, and erythritol, wherein the saccharide is present in a ratio of 4 to 30 parts by weight to 1 part by weight of the cyclic GMP phosphodiesterase inhibitor, as recited in the amended claim 1.

Thus, Bell-Huff '172 fails to anticipate the present invention. Withdrawal of the rejection is therefore respectfully requested.

Conclusion

Applicants respectfully submit that the above amendments and/or remarks fully address and overcome the rejections and objections of record. The instant claims are now in condition for allowance. Early and favorable action by the Examiner is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. 45,702) at the telephone number of the undersigned below.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of two (2) months to June 13, 2003, in which to file a reply to the Office Action. The required fee of $410.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional

fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By #32,881
John W. Bailey, #32,881

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Falls Church, VA 22040-0747
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JWB/KLR
0425-0832P

Attachments: Form PTO-1449
Version with markings to show changes made

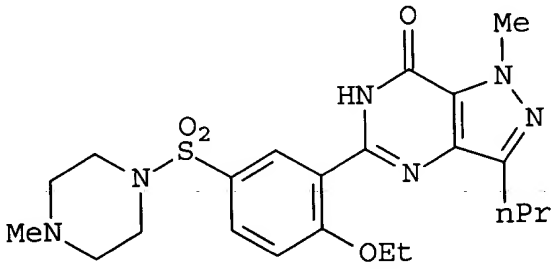
VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The following paragraphs are inserted into the specification on page 11, after line 2, but before line 3:

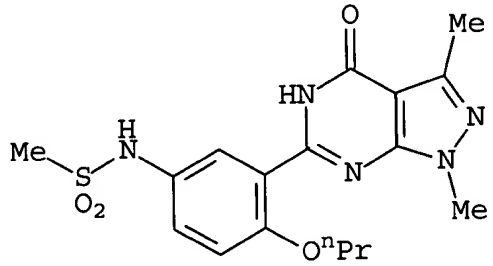
--The cyclic GMP phosphodiesterase inhibitor of the present invention may be selected from the group consisting of:

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one represented the formula (I)



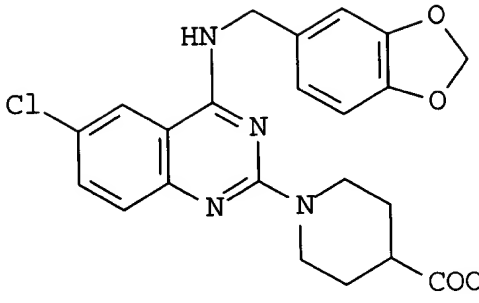
(I)

1,3-dimethyl-6-(2-propoxy-5-methanesulfonamidophenyl)-1,5-dihydropyrazolo[3,4-d]pyrimidin-4-one represented by the formula (II)



(II)

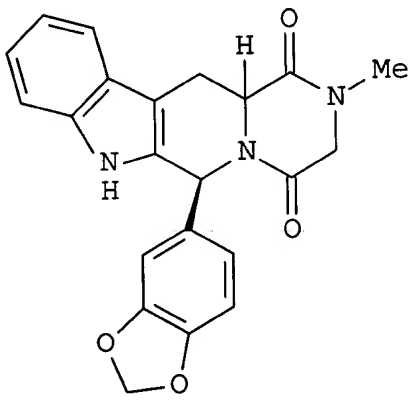
2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-chloroquinazoline represented by the formula (III)



(III)

,

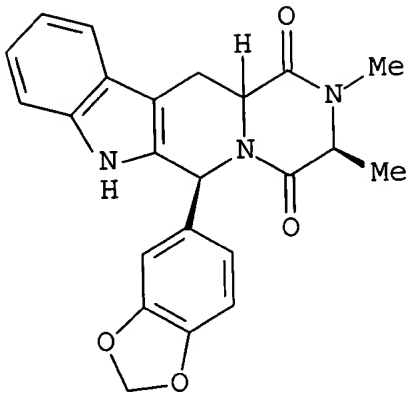
(6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]-indol-1,4-dione represented by the formula (IV)



(IV)

, and

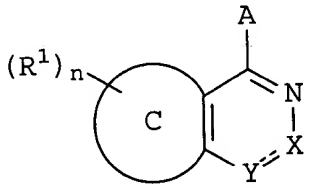
(3S,6R,12aR)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]-indol-1,4-dione shown by the formula (V)



(V)

or a pharmacologically acceptable salt thereof.

In addition, the cyclic GMP phosphodiesterase inhibitor may be a compound represented by the following formula (VI) or a pharmacologically acceptable salt thereof



(VI)

wherein in the formula,

the ring C is an unsaturated 5- or 6-membered ring which may have a hetero atom;

n is 0 or an integer of 1-4;

R^1 is a halogen atom, an optionally substituted lower alkyl group, an optionally substituted lower alkoxy group, an optionally substituted cycloalkyl group, nitro group, cyano group, a group represented by the formula $-NR^2R^3$, wherein

in the formula, R^2 and R^3 are the same as or different from each other and each is hydrogen atom, an optionally

substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group, R^2 and R^3 may form a ring together with a nitrogen atom bonded thereto, which ring may further have a substituent,

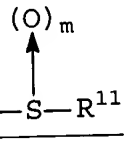
a group represented by the formula $-O-R^9$, wherein

in the formula, R^9 is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group,

a group represented by the formula $-S-R^{10}$, wherein

in the formula, R^{10} is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group,

a group represented by the formula (VII):



wherein in the formula (VII), R^{11} is hydrogen atom, a lower alkyl group or amino group; and m is 0 or an integer of 1-2,

or an optionally protected carboxyl group, and

when n is 2-4, R^1 may independently have the above-mentioned substituent;

A is hydrogen atom, a halogen atom, a group represented by the formula $-NR^4R^5$, wherein

in the formula, R^4 and R^5 are the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group, or R^4 and R^5 may form a ring together with a nitrogen atom bonded thereto, which ring may further have a substituent,

an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group;

X is a group represented by the formula $-NR^6-$, wherein

in the formula, R^6 is hydrogen atom, an optionally substituted lower alkyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group,

or a group represented by the formula -N=;

Y is a group represented by -CO- or a group represented by the formula -C(B)=, wherein

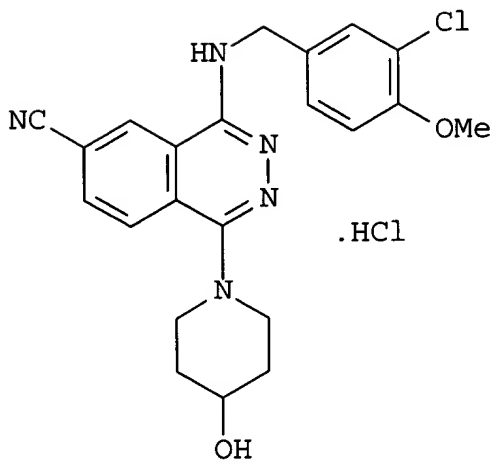
in the formula, B is hydrogen atom, a halogen atom, a formula represented by the formula $-NR^7R^8$, wherein in the formula, R^7 and R^8 may be the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted

arylalkyl group or an optionally substituted heteroarylalkyl group, R^7 and R^8 may form a ring together with a nitrogen atom bonded thereto, which ring may further have a substituent, a group represented by the formula $-O-R^{12}$, wherein in the formula, R^{12} is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group, a group represented by the formula $-S-R^{13}$, wherein in the formula, R^{13} is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group, an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group; and

the formula (VIII) ----- means a double or single bond, provided that when the ring C is a benzene ring, the case where n is 0 is excluded.

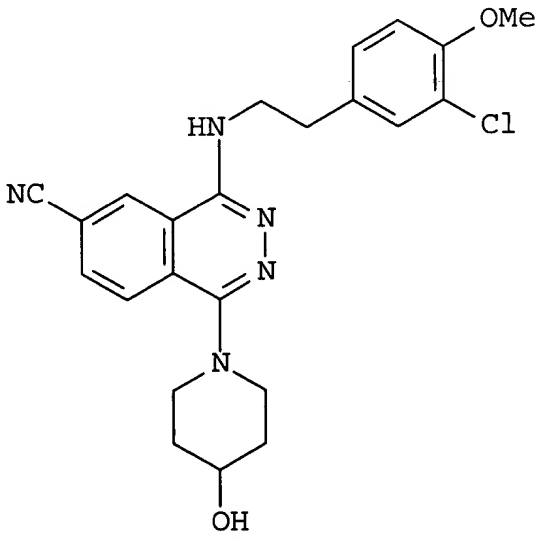
From the above, the compound represented by the formula (VI) may be selected from the group consisting of:

4-(3-chloro-4-methoxybenzyl)amino-6-cyano-1-(4-hydroxypiperidino)phthalazine hydrochloride represented by the formula (IX)



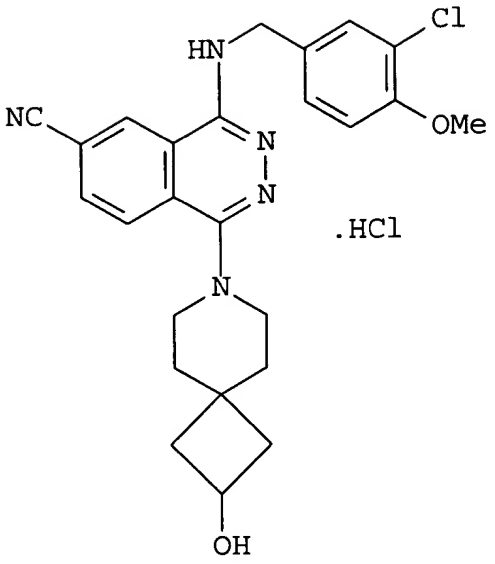
(IX)

4-(3-chloro-4-methoxyphenethyl)amino-6-cyano-1-(4-hydroxypiperidino)phthalazine hydrochloride represented by the formula (X)



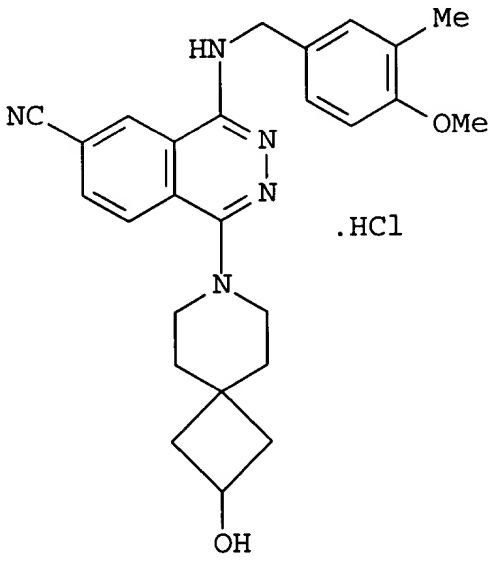
(X)

4-[(3-chloro-4-methoxybenzyl)amino]-1-(2-hydroxy-7-azaspiro[3,5]non-7-yl)-6-phthalazine carbonitrile hydrochloride represented by the formula (XI)



(XI)

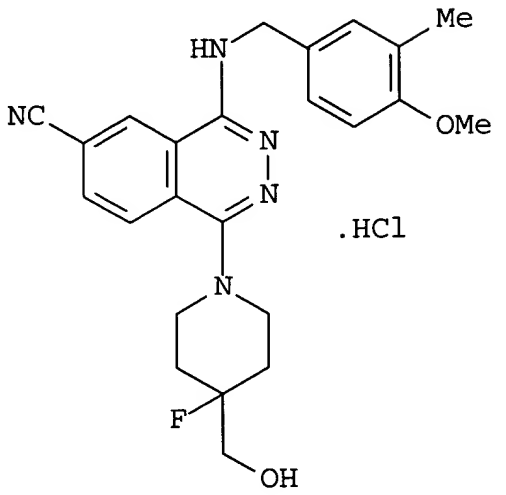
1-(2-hydroxy-7-azaspiro[3,5]non-7-yl)-4-[(4-methoxy-3-methylbenzyl)amino]-6-phthalazine carbonitrile hydrochloride represented by the formula (XII)



(XII)

1-[4-fluoro-4-(hydroxymethyl)piperidino]-4-[(4-methoxy-3-methylbenzyl)amino]-6-phthalazine carbonitrile hydrochloride

represented by the formula (XIII)



(XIII)

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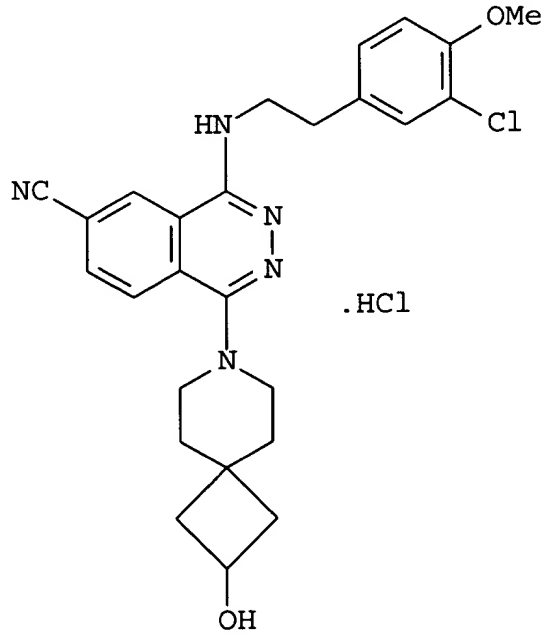
4-[(3-chloro-4-methoxyphenethyl)amino]-1-(2-hydroxy-7-azaspiro[3,5]non-7-yl)-6-phthalazine carbonitrile hydrochloride shown by the formula (XIV)

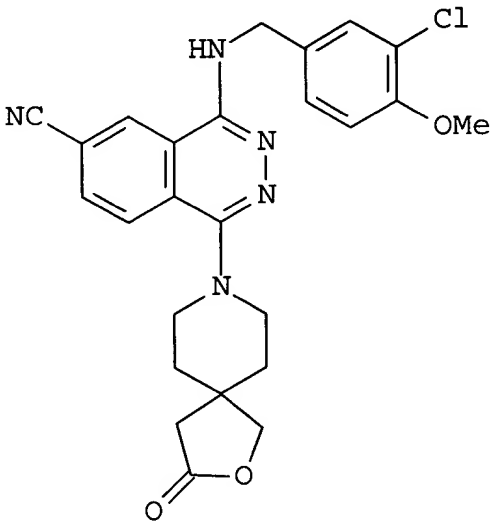


(XIV)

, and

4-[(3-chloro-4-methoxybenzyl)amino]-1-(3-oxo-2-oxa-8-

azaspiro[4,5]decen-8-yl)-6-phthalazine carbonitrile represented by the formula (XV)



(XV)

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In the claims:

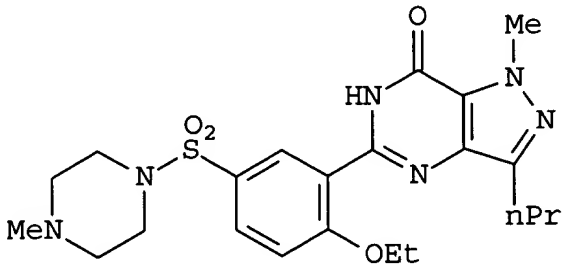
The claims are amended as follows:

1. (Amended) An intraoral quickly disintegrating tablet comprising a cyclic GMP phosphodiesterase inhibitor and a saccharide selected from the group consisting of mannitol, xylitol, and erythritol,

wherein the saccharide is present in a ratio of 4 to 30 parts by weight to 1 part by weight of the cyclic GMP phosphodiesterase inhibitor.

13. (Amended) The [tablets] tablet as claimed in any one of claims 1, 2 and 11, wherein the cyclic GMP phosphodiesterase inhibitor is selected from the group consisting of:

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one represented the formula (I)



(I)

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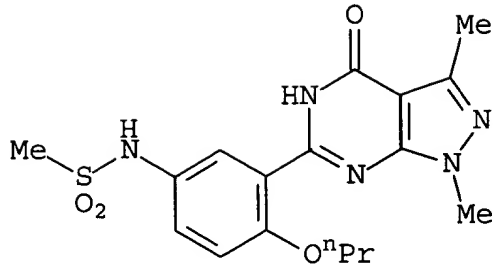
1,3-dimethyl-6-(2-propoxy-5-methanesulfonamidophenyl)-1,5-dihydropyrazolo[3,4-d]pyrimidin-4-one represented by the formula (II)



(II)

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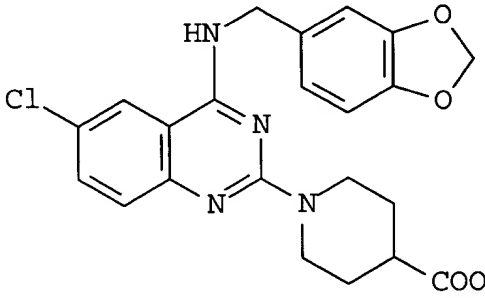
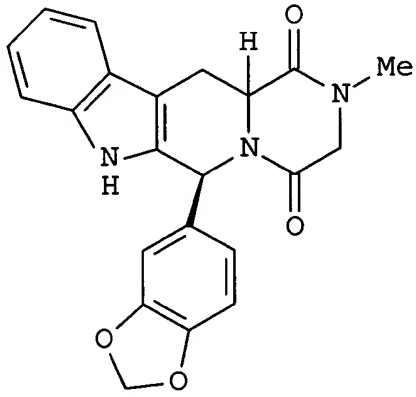
2-(4-carboxypiperidino)-4-(3,4-methylenedioxybenzyl)amino-6-chloroquinazoline represented by the formula (III)



(III)

---,

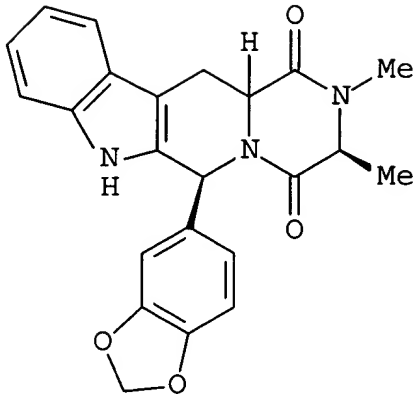
(6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]-indol-1,4-dione represented by the formula (IV)



(IV)

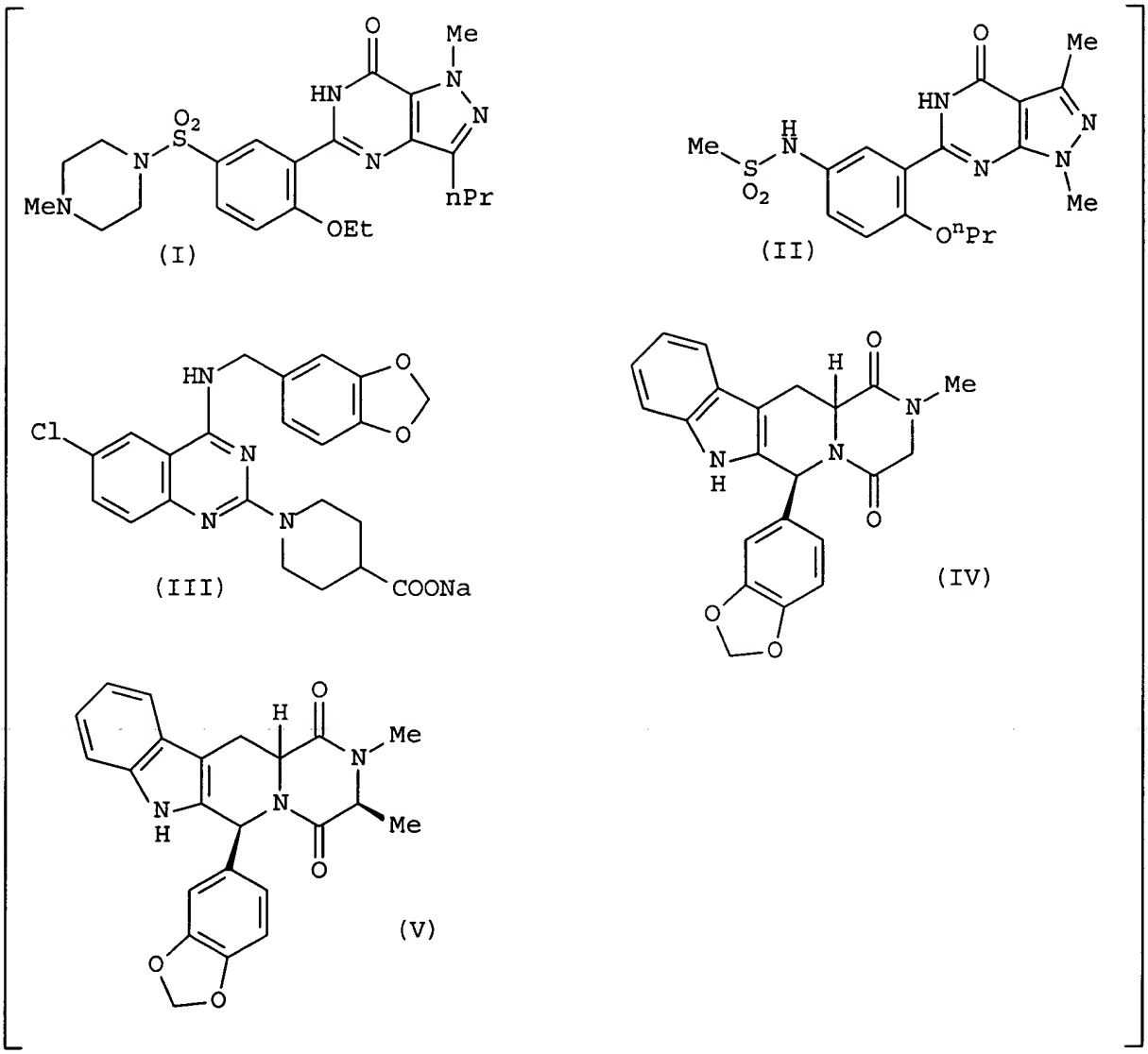
---, and

(3S,6R,12aR)-2,3,6,7,12,12a-hexahydro-2,3-dimethyl-6-(3,4-methylenedioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]-indol-1,4-dione shown by the formula (V)

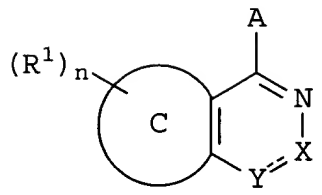


(V)

or a pharmacologically acceptable salt thereof.



14. (Amended) The tablet as claimed in any <u>one</u> of claims 1, 2 and 11, wherein the cyclic GMP phosphodiesterase inhibitor is a compound represented by the following formula (VI) or a pharmacologically acceptable salt thereof[, i.e. a fused pyridazine compound represented by the following formula or a pharmacologically acceptable salt thereof.]



(VI)

wherein in the formula,

the ring C is an unsaturated 5- or 6-membered ring which may have a hetero atom;

n is 0 or an integer of 1-4;

R^1 is a halogen atom, an optionally substituted lower alkyl group, an optionally substituted lower alkoxy group, an optionally substituted cycloalkyl group, nitro group, cyano group, a group represented by the formula $-NR^2R^3$, wherein

[(] in the formula, R^2 and R^3 are the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[.], R^2 and R^3 may form a ring together with a nitrogen atom bonded thereto, which[. The] ring may further have a substituent[)],

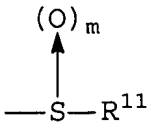
a group represented by the formula $-O-R^9$, wherein

[(]in the formula, R^9 is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[(],

a group represented by the formula $-S-R^{10}$, wherein

[(]in the formula, R^{10} is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[(],

a group represented by the formula (VII):



wherein [(]in the formula (VII), R^{11} is hydrogen atom, a lower alkyl group or amino group; and m is 0 or an integer of 1-2[(],

or an optionally protected carboxyl group, and

when n is 2-4, R^1 may independently have the above-mentioned substituent;

A is hydrogen atom, a halogen atom, a group represented by the formula $-NR^4R^5$, wherein [(]

in the formula, R^4 and R^5 are the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group, or R^4 and R^5 may form a ring together with a nitrogen atom bonded thereto, which[. The] ring may further have a substituent[(],

an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted arylalkyl

group or an optionally substituted heteroarylalkyl group;

X is a group represented by the formula $-NR^6-$, wherein

[(]in the formula, R^6 is hydrogen atom, an optionally substituted lower alkyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[(],

or a group represented by the formula -N=;

Y is a group represented by -CO- or a group represented by the formula -C(B)=, wherein

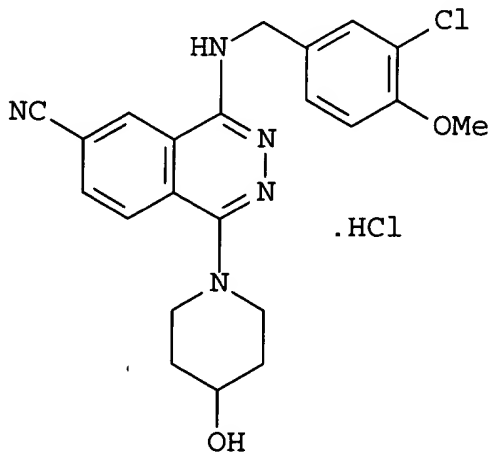
[(]in the formula, B is hydrogen atom, a halogen atom, a formula represented by the formula $-NR^7R^8$, wherein [(]in the formula, R^7 and R^8 may be the same as or different from each other and each is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[.], R^7 and R^8 may form a ring together with a nitrogen atom bonded thereto[. The], which ring may further have a substituent[(], a group represented by the formula $-O-R^{12}$, wherein [(]in the formula, R^{12} is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[)], a group represented by the formula $-S-R^{13}$, wherein [(]in the formula, R^{13} is hydrogen atom, an optionally substituted lower alkyl group, an acyl group, an optionally substituted

arylalkyl group or an optionally substituted heteroarylalkyl group[)], an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted arylalkyl group or an optionally substituted heteroarylalkyl group[)]; and

the formula (VIII) ----- means a double or single bond, provided that when the ring C is a benzene ring, the case where n is 0 is excluded.

15. (Amended) The tablet as claimed in claim 14, wherein the compound represented by the formula (VI) is selected from the group consisting of:

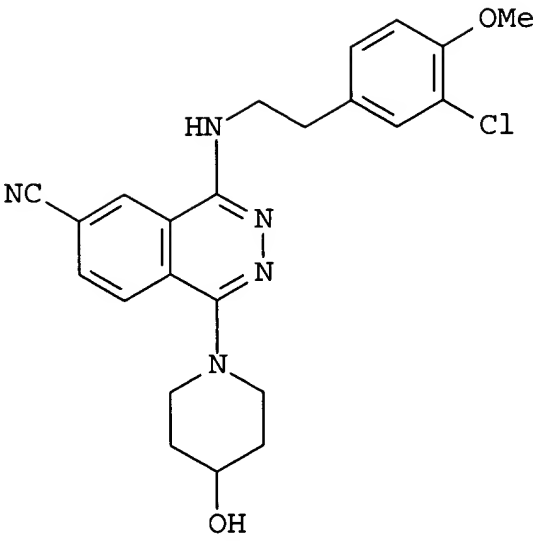
4-(3-chloro-4-methoxybenzyl)amino-6-cyano-1-(4-hydroxypiperidino)phthalazine hydrochloride represented by the formula (IX)



(IX)

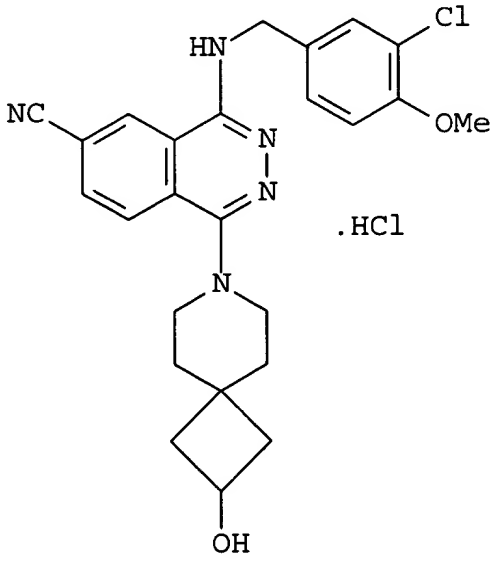
4-(3-chloro-4-methoxyphenethyl)amino-6-cyano-1-(4-hydroxypiperidino)phthalazine hydrochloride represented by the

formula (X)



(X)

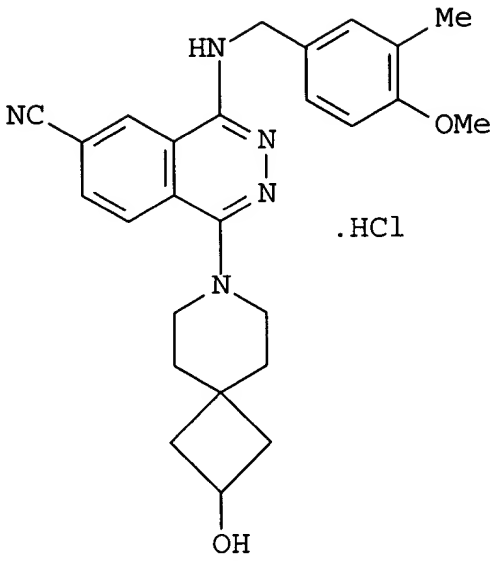
4-[(3-chloro-4-methoxybenzyl)amino]-1-(2-hydroxy-7-azaspiro[3,5]non-7-yl)-6-phthalazine carbonitrile hydrochloride represented by the formula (XI)



(XI)

1-(2-hydroxy-7-azaspiro[3,5]non-7-yl)-4-[(4-methoxy-3-methylbenzyl)amino]-6-phthalazine carbonitrile hydrochloride

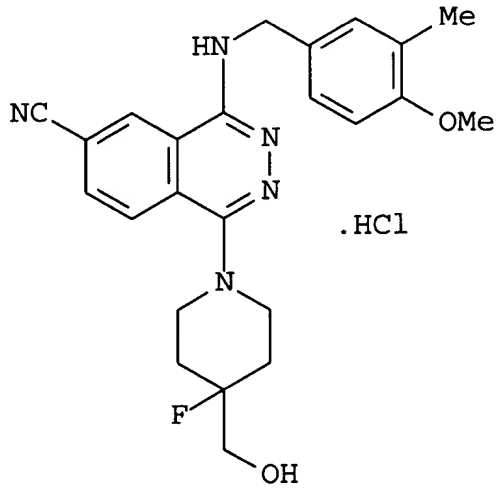
represented by the formula (XII)



(XII)

,

1-[4-fluoro-4-(hydroxymethyl)piperidino]-4-[(4-methoxy-3-methylbenzyl)amino]-6-phthalazine carbonitrile hydrochloride represented by the formula (XIII)

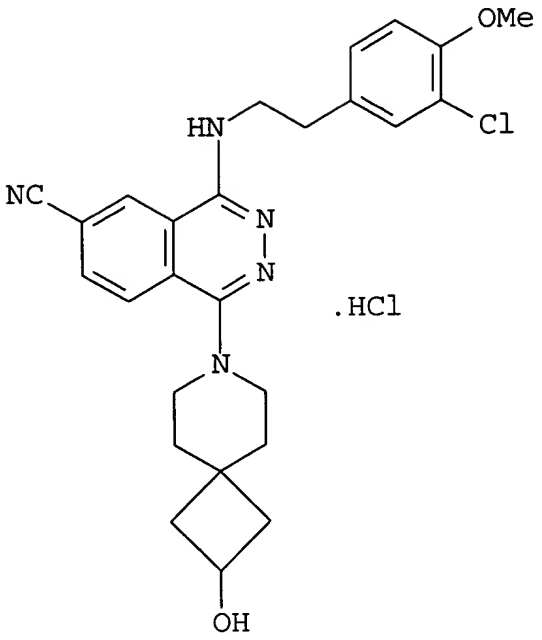


(XIII)

,

4-[(3-chloro-4-methoxyphenethyl)amino]-1-(2-hydroxy-7-azaspiro[3,5]non-7-yl)-6-phthalazine carbonitrile hydrochloride

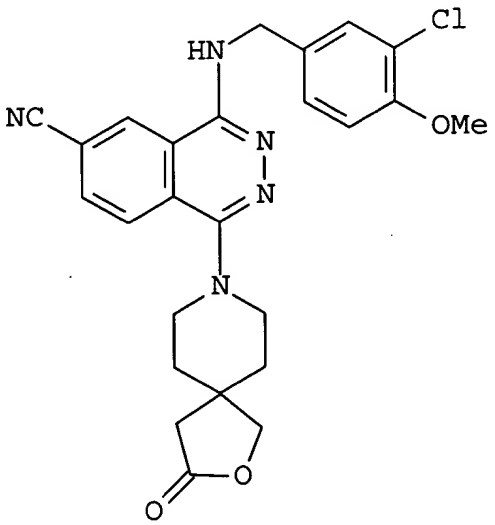
shown by the formula (XIV)



(XIV)

[or] , and

4-[(3-chloro-4-methoxybenzyl)amino]-1-(3-oxo-2-oxa-8-azaspiro[4,5]decen-8-yl)-6-phthalazine carbonitrile represented by the formula (XV)



(XV)

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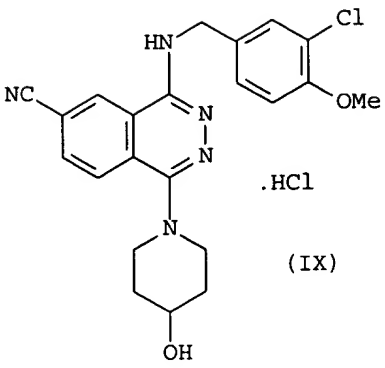
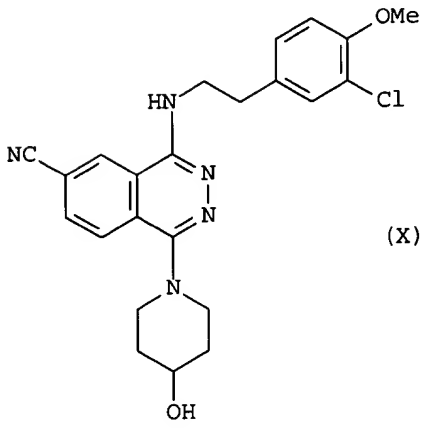
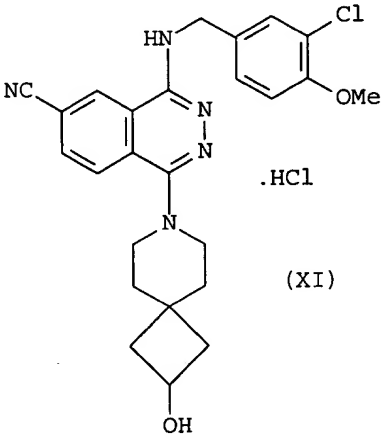


.HCl

(IX)

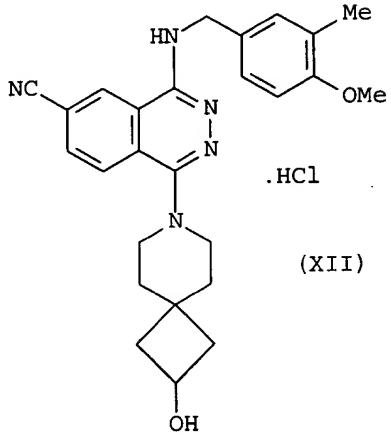


(X)



.HCl

(XI)



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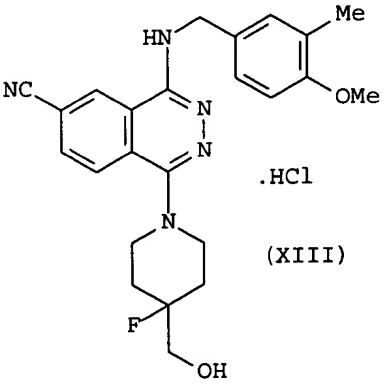
(XII)



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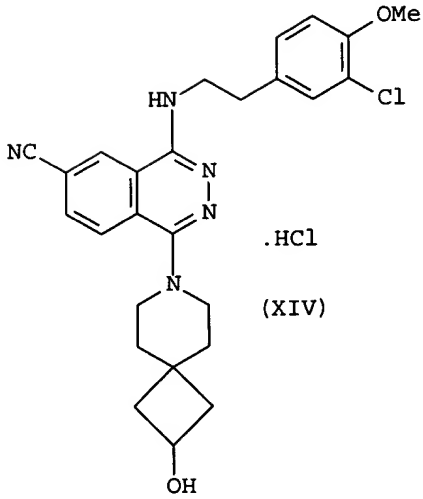
(XIII)



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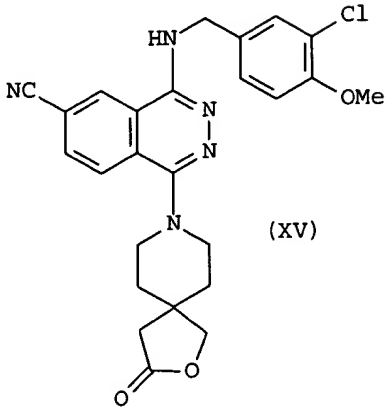
(XIV)



(XV)

17. (Amended) The method for manufacturing as claimed in any one of claims 3[,] and 4 [and 12], wherein the cyclic GMP phosphodiesterase inhibitor is selected from the group consisting of:

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulfonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one represented by the formula (I), and

a compound represented by the formula (VI),

or pharmacologically acceptable salts thereof.